Claims After Amendment - U.S. Patent Application No. 10/060,941

1. A method of screening a candidate antiviral agent for antiviral activity comprising

(a) preparing a first cell culture comprising cells containing a first subgenomic viral replication system, and a second cell culture comprising cells containing a second subgenomic viral replication system;

(b) adding the candidate antiviral agent to each cell culture;

(c) incubating the cell cultures under conditions and for a time sufficient to detect an antiviral effect by the candidate antiviral agent on the subgenomic viral replication systems; and

(d) determining the effect of the candidate antiviral agent on each viral replication system,

wherein the first subgenomic viral replication system is genetically distinct from the second subgenomic viral replication system.

2. The method of claim 1, wherein the first and second cell cultures are combined before step (b).

3. The method of claim 1, further comprising a cell culture not containing a subgenomic viral replication system.

4. The method of claim 1, wherein at least one of the subgenomic viral replication systems is a replicon.

5. The method of claim 1, wherein at least one of the subgenomic viral replication systems is a defective genome.

6. The method of claim 1, wherein the cells in the first and second cell cultures are mammalian cells and the first and second subgenomic viral replication systems are

from mammalian viruses.

7. The method of claim 6, wherein the mammalian cells are human cells and the mammalian viruses are human viruses.

8. The method of claim 7, wherein the human viruses are selected from the group consisting of hepatitis C virus, yellow fever virus, respiratory syncytia virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, adeno-associated virus, Venezuela encephalitis virus, rubella, coxsackivirus, enterovirus, hepatitis A virus, Dengue fever virus, West Nile virus, tick-borne encephalitis virus, astrovirus, rabies virus, influenza virus A, influenza virus B, respiratory syncytial virus, measles, mumps, Ebola virus, Marburg virus, La Crosse virus, California encephalitis virus, Hantaan virus, Crimean-Congo virus, Rift Valley fever, Lassa fever, Argentine hemorrhagic fever virus, Bolivian hemorrhagic fever virus, Colorado tick fever, JC virus, BK virus, herpes simplex virus type two, human cytomegalovirus, varicella-zoster virus, human herpes simplex virus type six, human herpes virus type seven, human herpes virus type eight, human adenovirus, HIV-1, HIV-2, HTLV-1, HTLV-2, and human parvovirus.

9. The method of claim 7, wherein the human viruses are selected from the group consisting of hepatitis C virus, yellow fever virus, respiratory syncytia virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, and adeno-associated virus.

10. The method of claim 7, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus and Sindbis virus.

26. The method of claim 1, further comprising at least a third cell culture comprising cells containing a third subgenomic viral replication system, wherein the third cell culture is also subjected to steps (a), (b), (c) and (d),

wherein the each subgenomic viral replication system is genetically distinct from every other subgenomic viral replication system.

27. The method of claim 26, wherein all cell cultures comprising a subgenomic viral replication system are combined before step (b).

55. A mixed cell culture comprising a first cell culture comprising cells containing a first subgenomic viral replication system and a second cell culture comprising cells containing a second subgenomic viral replication system.

56. The mixed cell culture of claim 55, wherein at least one of the subgenomic viral replication systems is a replicon.

57. The mixed cell culture of claim 55, wherein at least one of the subgenomic viral replication systems is a defective genome.

58. The mixed cell culture of claim 55, wherein all of the cells of the mixed cell culture are the same cell line.

59. The mixed cell culture of claim 55, wherein the cells of the mixed cell culture comprise more than one cell line.

60. The mixed cell culture of claim 55, wherein all of the cells in the mixed cell culture are mammalian cells and all of the subgenomic viral replication systems are from

mammalian viruses.

61. The mixed cell culture of claim 60, wherein the mammalian cells are human cells and the mammalian viruses are human viruses.

62. The mixed cell culture of claim 61, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, adeno-associated virus, Venezuela encephalitis virus, rubella, coxsackivirus, enterovirus, hepatitis A virus, Dengue fever virus, West Nile virus, tick-borne encephalitis virus, astrovirus, rabies virus, influenza virus A, influenza virus B, respiratory syncytial virus, measles, mumps, Ebola virus, Marburg virus, La Crosse virus, California encephalitis virus, Hantaan virus, Crimean-Congo virus, Rift Valley fever, Lassa fever, Argentine hemorrhagic fever virus, Bolivian hemorrhagic fever virus, Colorado tick fever, JC virus, BK virus, herpes simplex virus type two, human cytomegalovirus, varicella-zoster virus, human herpes simplex virus type six, human herpes virus type seven, human herpes virus type eight, human adenovirus, HIV-1, HIV-2, HTLV-1, HTLV-2, and human parvovirus.

63. The mixed cell culture of claim 61, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, and adeno-associated virus.

64. The mixed cell culture of claim 61, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever

virus and Sindbis virus.

68. The mixed cell culture of claim 55, further comprising a third cell culture comprising cells containing a third subgenomic viral replication system.

69. The mixed cell culture of claim 68, wherein the mixed cell culture further comprises a fourth cell culture comprising cells containing a fourth subgenomic viral replication system.